

REMARKS

Entry of this amendment is respectfully requested.

Claims 29-32 and 34-53 were pending in this application. In this response, claims 29-32, 34, 37, 38, 41, and 42 are cancelled (claims 29-32 and 34 as being directed to a non-elected invention), and claims 35, 40, and 51-53 are amended for further clarity. Support for the amendments can be found in the specification and claims as originally filed. For example, administration of 10 ug estradiol twice weekly is disclosed, e.g., at page 5, lines 9-11. No new matter is added. Accordingly, claims 35, 36, 39, 40, and 43-53 are pending and at issue.

Claim 53 has been objected to for the use of a double colon. This claim is amended herein, obviating this objection.

Rejections Under 35 U.S.C. § 112

Claims 35-53 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that the specification does not provide support for the use of estradiol derivatives other than estradiol. This rejection is respectfully traversed.

Applicants believe that one of ordinary skill in the art would recognize that therapeutically equivalent estrogens could be used in practicing the present invention in place of estradiol without undue experimentation. Nonetheless, to expedite prosecution, the claims have been amended to encompass estradiol. It is respectfully submitted on this basis that this rejection has been overcome.

Claims 35-53 have been rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness, for (i) the recitation of “derivatives” (claims 35, 37-42, and 49); and (ii) the recitation of “low” (claim 51). These rejections are respectfully traversed.

It is believed that therapeutically equivalent estradiol derivatives are known and understood in the art. Nonetheless, to expedite prosecution the claims have been amended to delete the term “derivative”. Furthermore, claim 51 has been amended to delete the term “low”. It is respectfully submitted on this basis that these rejections have been overcome.

Rejection Under 35 U.S.C. § 102

Claims 35-37, 43-48, 52-53 have been rejected under 35 U.S.C. §102(b) as anticipated by Mettler et al., *Maturitus* 14:23, 1991. This rejection is respectfully traversed.

The present claims encompass the treatment of atrophic vaginitis by once- or twice-weekly administration of 10 ug estradiol (claim 35); twice-weekly administration of 5 ug estradiol (claim 40), or daily administration of 2-3 ug estradiol (claim 39).

Mettler et al. relates to the administration of much higher doses of estradiol (i.e., at least 25 ug/week.) Accordingly, Mettler et al. cannot anticipate the invention as presently claimed, and this rejection should be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 35, 38-42, and 49-51 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Mettler et al., in view of Meignant (WO 97/12600) and Vagifem® monograph (Novo Nordisk® 2000). The Examiner contends that Mettler et al. discloses the use of estradiol to treat atrophic vaginitis; that Meignant discloses the use of dosages having less than 10 ug estradiol; that the Vagifem® monograph discloses tablets containing estradiol; and that it would have been obvious to combine the teachings of these citations to achieve the presently-claimed invention. This rejection is respectfully traversed.

The present invention is based on the finding that low aggregate doses of estradiol can be useful in treating symptoms associated with atrophic vaginitis. For example, the studies described in Examples 1-3 of the present specification clearly demonstrate that twice-weekly intravaginal administration of 10 ug estradiol tablets resulted in significant therapeutic benefit without significant side effects (see, e.g., Figure 6).

Mettler et al. relates to higher doses of estradiol than those encompassed by the present claims. Meignant relates to particular types of formulations that have bioadhesive properties and thereby provide estradiol to the vaginal mucosa for longer times; thus, Meignant implicates higher dosages than those encompassed by the present claims as necessary to provide therapeutic efficacy. Notably, Meignant does not disclose any clinical results that would support the use of low doses of estradiol to relieve symptoms of atrophic vaginitis. Accordingly, nothing in the cited references, taken either singly or in combination, could have provided one of ordinary skill in the art with any reasonable expectation of achieving the benefits of the present invention.

On this basis, it is respectfully submitted that the presently claimed invention is non-obvious over the cited references and that this rejection should be withdrawn.

It is believed that the claims are in condition for allowance, and a determination to
that effect is earnestly solicited.

Respectfully submitted,



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